

IN THE SPECIFICATION:

Please amend the paragraph beginning on page 9, line 18 as follows:

~~Figure 3~~ Figures 3A to 3K is a representation of the nucleotide sequence from various strains of HBV encoding the surface antigen. The amino acid sequence of the surface antigen beginning at amino acid 108, as set forth in SEQ ID NO: 23, is shown above the nucleotide sequence.

Please amend the paragraph beginning on page 9, line 28 as follows:

Figures 5A to 5F is the representation of the nucleotide sequence of HBV 1.28 genome.

Please amend the paragraph beginning on page 9, line 30 as follows:

~~Figure 5B~~ Figures 14A to 14F is the representation of the nucleotide sequence of HBV 1.5 genome.

Please amend the paragraph beginning on page 10, line 20 as follows:

Figures 11A to 11E~~11F~~ are photographic representations showing Southern blot of the intracellular and extracellular HBV DNA production from HepG2 cells transduced with wildtype (WT) and precore (G1 896A) recombinant HBV-baculovirus exposed to increasing concentrations of (A) adefovir, (B) lamivudine and (C) penciclovir. IC, intracellular; EC, extracellular; RC, relaxed circular HBV DNA; DS, linear double-stranded HBV DNA; SS, single-stranded HBV DNA.

Please amend the paragraph beginning on page 11, line 1 as follows:

Figures 13A to 13F~~13L~~ are photographic representations showing Southern blot of intracellular and extracellular HBV DNA production from HepG2 cells transduced with recombinant HBV-Baculovirus [M550I and precore/M550I (Figures 13A, 13B, ~~13C~~13E, 13F,

13I, 13J] L526M/M550V and precore/L526M/M550V (Figures 13B, 13D, 13F~~13C, 13D, 13G,~~

13H, 13K 13L] exposed to various concentrations of adefovir, or lamivudine, or penciclovir.

The extracellular virus production from cells transduced with L526M/M550V was to olow to be measured. IC, intracellular; EC, extracellular; RC, relaxed circular HBV DNA; DS, linear double-stranded HBV DNA; SS, single-stranded HBV DNA.

Please amend the paragraph beginning on page 40, line 20 as follows:

The nucleotide sequence from various strains of HBV encoding the surface antigen is shown in Figure 3~~Figures 3A to 3K~~. The amino acid sequence of the surface antigen beginning at amino acid 108 is shown above the nucleotide sequence.

Please amend the paragraph beginning on page 43, line 7 as follows:

The sequence of the 1.28 and the 1.5 HBV genome (Figures 5A and 5B~~to 5F and Figures 14A to 14F~~, respectively) were elucidated using the ABI Prism Big Dye Terminator Cycle Sequencing Ready Reaction Kit according to the manufacturer's specifications (Perkin Elmer, Cetus Norwalk, CT).

Please amend the paragraph beginning on page 53, line 5 as follows:

In this study, comparable HBV DNA production by wild-type (1.3 x genomic length HBV) and the precore mutant of HBV was found using the recombinant HBV-baculovirus system. The dose effect of lamivudine, adefovir, and penciclovir on the wild-type HBV/baculovirus virus and the precore mutant (G1986A) HBV are shown in Figure 11 (A, B, C~~Figures 11A to 11F~~) and the calculated IC₅₀ is shown in Table 3. HBV with the specific mutation of G1986A seemed to be at lest as sensitive for adefovir, and may be more sensitive to lamivudine and penciclovir compared with wild type HBV.

Please amend the paragraph beginning on page 53, line 26 as follows:

Intracellular HBV DNA and extracellular virus produced by HepG2 cells transduced with various recombinant HBV-baculovirus (including M550I, precore/M550I, L526M/M550V and precore/L526M/L550V) in the presence of adefovir, or lamivudine or penciclovir are shown in Figure 13 (A-F)Figures 13A to 13L and the calculated IC₅₀ for adevoir is shown in Table 4. The adefovir concentration required to inhibit HBV replication (intracellular single-stranded DNA) by 50% (IC₅₀) was 0.94 µM and 0.93 µM for the recombinant HBV-baculovirus mutants M550I and L526M/M550V respectively, and 0.28 µM and 0.47 µM for precore /M550I and precore/L526M/M550V respectively. The Southern blots of intracellular HBV replicative intermediates and extracellular virus produced by HepG2 cells transduced with respective recombinant HBV-baculovirus showed that for any HBB/baculovirus variant encoding the mutations at M550I or L526M/M550V changes conferred a high degree of resistance to lamivudine and penciclovir and no dose response could be plotted.

Amendments to the Drawings:

Please replace the drawings of record with the attached substitute drawings

Figures 1 to 14F.